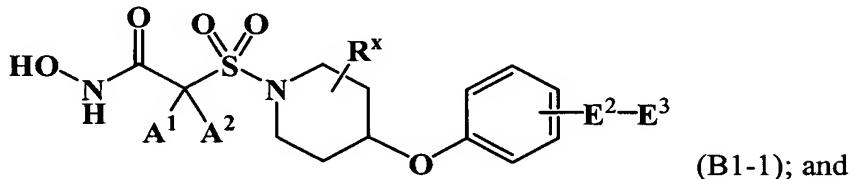


We claim:

1. A compound or a salt thereof, wherein:
the compound corresponds in structure to the following formula:



A^1 and A^2 are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclylalkoxyalkyl, carbocyclylalkylthio, carbocyclylthioalkyl, carbocyclylalkylthioalkyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, heterocyclyoxyalkyl, heterocyclalkoxyalkyl, heterocyclalkylthio, heterocyclalkylthioalkyl, and heterocyclalkylthioalkyl, wherein:

any member of such group optionally is substituted with up to 3

independently selected R^X substituents; and

15 each R^X is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy, R^a -oxyalkyl, alkenyloxy, alkynyoxy, alkylthio, alkylsulfonyl, R^aR^a -amino, R^aR^a -aminoalkyl, R^aR^a -aminoalkoxy, R^aR^a -aminoalkyl(R^a)amino, R^aR^a -aminosulfonyl, carbocyclyl, carbocyclylalkyl, carbocyclloxy, carbocyclloxyalkoxy, carbocyclylthio, 20 carbocyclsulfonyl, heterocyclyl, heterocyclylalkyl, heterocyclloxy, heterocyclloxyalkoxy, heterocyclylthio, and heterocyclsulfonyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

the amino optionally is substituted with up to 2 independently selected alkyl; and

E² is selected from the group consisting of -C(O)-, -C(O)-O-, -O-C(O)-, -N(R^a)-, -C(O)-N(R^a)-, -N(R^a)-C(O)-, -C(O)-N(R^a)-N(R^a)-C(O)-, -S-, -S(O)-, -S(O)2-, -N(R^a)-S(O)2-, -S(O)2-N(R^a)-, -O-S(O)2-, -S(O)2-O-, -C(NH)-, and -C(NOH)-; and

E³ is selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxyalkoxyalkyl, alkylthioalkyl, alkylthioalkylthioalkyl, alkylthioalkoxyalkyl, alkoxyalkylthioalkyl, aminoalkyl, carbocyclyl, carbocyclylalkyl, heterocyclyl, and heterocyclylalkyl, wherein:

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, hydroxyimino, amino (optionally substituted with up to two substituents independently selected from alkyl and carbocyclylalkyl), alkyl, alkoxy, alkylthio, carbocyclyl, and carbocyclylalkyl, wherein:

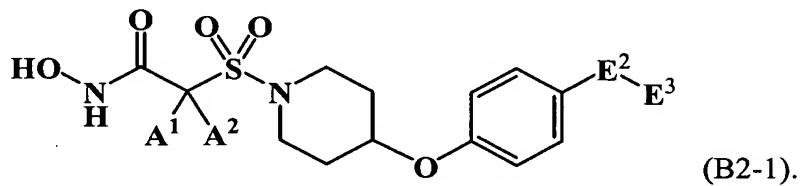
any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino; and

each R^a is independently selected from the group consisting of hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl, alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl, carbocyclylalkyl, carbocyclyoxyalkyl, carbocyclalkoxyalkyl, carbocyclthioalkyl, carbocyclthioalkenyl, carbocyclsulfoxidoalkyl, carbocyclsulfonyl, carbocyclsulfonylalkyl, heterocyclyl, heterocyclalkyl, heterocyclalkoxyalkyl, heterocyclthioalkyl, heterocyclsulfoxidoalkyl, heterocyclsulfonyl, heterocyclsulfonylalkyl, aminoalkyl, aminosulfonyl, aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein any member of such group optionally is substituted:

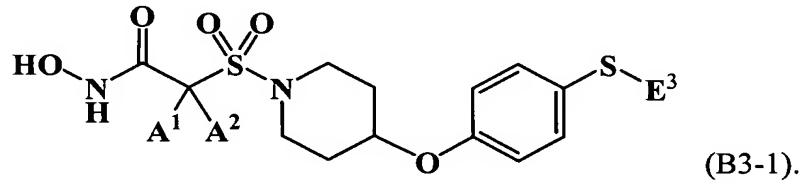
on any carbon atom(s) capable of such substitution with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, and imino, and

5 on any amino nitrogen atom with up to 2 substituents independently selected from the group consisting of alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl.

2. A compound or salt thereof according to claim 1, wherein the compound corresponds in structure to the following formula:



3. A compound or salt thereof according to claim 2, wherein the compound corresponds in structure to the following formula:



15 4. A compound or salt thereof according to claim 3, wherein E³ is alkyl optionally substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, hydroxyimino, amino (optionally substituted with up to two substituents independently selected from alkyl and carbocyclylalkyl), alkyl, alkoxy, alkylthio, carbocyclyl, and carbocyclylalkyl, wherein:

20

any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and amino.

25

5. A compound or salt thereof according to claim 4, wherein E³ is alkyl substituted with one or more independently selected halogen.

5 6. A compound or salt thereof according to claim 5, wherein E³ is C₁-C₄-alkyl substituted with one or more fluoro.

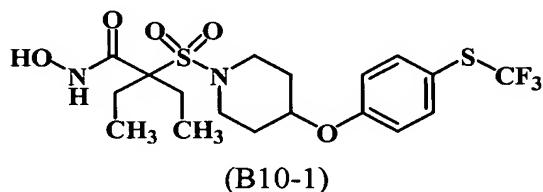
7. A compound or salt thereof according to claim 6, wherein E³ is trifluoromethyl.

10 8. A compound or salt thereof according to claim 3, wherein A¹ and A² are independently selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₁-C₃-alkoxy-C₁-C₃-alkyl, C₁-C₃-alkylthio-C₁-C₃-alkyl, C₂-C₆-alkenyl, and C₂-C₆-alkynyl.

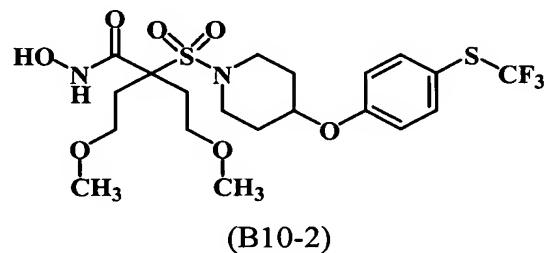
9. A compound or salt thereof according to claim 8, wherein:

15 A¹ and A² are independently selected from the group consisting of methyl, ethyl, and methoxyethyl; and
E³ is C₁-C₄-alkyl substituted with one or more independently selected halogen.

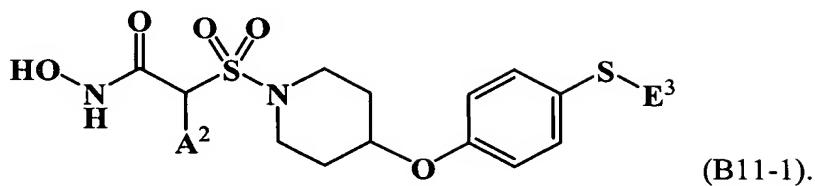
10. A compound or salt thereof according to claim 9, wherein the compound
20 corresponds in structure to a formula selected from the group consisting of:



and



11. A compound or salt thereof according to claim 3, wherein the compound corresponds in structure to the following formula:



12. A compound or salt thereof according to claim 11, wherein A² is selected from the group consisting of C₁-C₆-alkyl, C₁-C₃-alkoxy-C₁-C₃-alkyl, C₁-C₃-alkylthio-C₁-C₃-alkyl, C₂-C₆-alkenyl, and C₂-C₆-alkynyl.

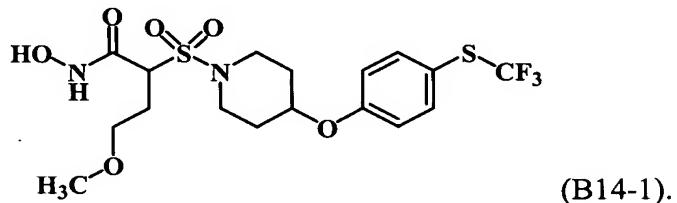
5

13. A compound or salt thereof according to claim 12, wherein:

A² is selected from the group consisting of methyl, ethyl, and methoxyethyl; and E³ is C₁-C₄-alkyl substituted with one or more independently selected halogen.

10

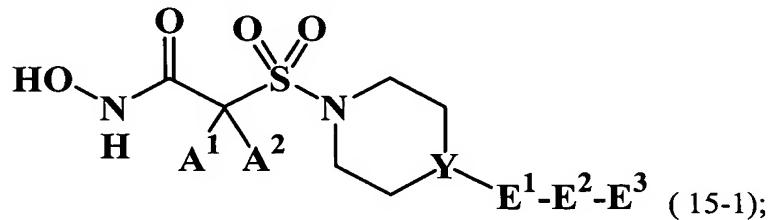
14. A compound or salt thereof according to claim 13, wherein the compound corresponds in structure to the following formula:



15

15. A compound or a salt thereof, wherein:

the compound corresponds in structure to the following formula:



as to A¹ and A²:

A¹ and A², together with the carbon to which they are bonded, form

20 heterocyclyl or carbocyclyl, wherein:

the heterocyclyl and carbocyclyl optionally are substituted with up to 3 independently selected R^X substituents, or

5 A^1 and A^2 are independently selected from the group consisting of hydrogen, alkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, alkynyl, carbocyclyl, carbocyclylalkyl, carbocyclylalkenyl, carbocyclylalkynyl, carbocyclyoxyalkyl, carbocyclalkoxyalkyl, carbocyclalkylthio, carbocyclthioalkyl, carbocyclalkylthioalkyl, heterocyclyl, heterocyclalkyl, heterocyclalkenyl, heterocyclalkynyl, heterocyclyoxyalkyl, heterocyclalkoxyalkyl, heterocyclalkylthio, heterocyclthioalkyl, and heterocyclalkylthioalkyl,

10 wherein:

any member of such group optionally is substituted with up to 3 independently selected R^X substituents; and

each R^X is independently selected from the group consisting of halogen, cyano, hydroxy, nitro, nitroso, oxo, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, alkoxyalkoxy,

15 R^a -oxyalkyl, alkenyloxy, alkynyoxy, alkylthio, alkylsulfonyl, R^aR^a -amino, R^aR^a -aminoalkyl, R^aR^a -aminoalkoxy, R^aR^a -aminoalkyl(R^a)amino, R^aR^a -aminosulfonyl, carbocyclyl, carbocyclylalkyl, carbocyclyoxy, carbocyclyoxyalkoxy, carbocyclthio, carbocyclsulfonyl, heterocyclyl, heterocyclalkyl, heterocycloxy, heterocycloxyalkoxy, heterocyclthio, and heterocyclsulfonyl, wherein:

20 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, amino, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, alkyl, alkoxy, alkoxyalkyl, and alkoxyalkoxy, wherein:

25 any member of such group optionally is substituted with one or more substituents independently selected from the group consisting of halogen and hydroxy, and

 the amino optionally is substituted with up to 2 independently selected alkyl; and

Y is selected from the group consisting of nitrogen and carbon bonded to

30 hydrogen; and

E¹ is selected from the group consisting of alkyl and alkenyl, wherein:
the alkyl and alkenyl are optionally substituted with one or more
substituents independently selected from the group consisting of halogen, hydroxy,
amino, mono-alkylamino, di-alkylamino, nitro, nitroso, alkyl, alkoxy, alkoxyalkyl,
and alkylthio, wherein:

any member of such group optionally is substituted with one or
more substituents independently selected from the group consisting of
halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo,
and imino; and

10 E² is selected from the group consisting of -O-, -C(O)-, -C(O)-O-, -O-C(O)-,
-N(R^a)-, -C(O)-N(R^a)-, -N(R^a)-C(O)-, -C(O)-N(R^a)-N(R^a)-C(O)-, -N(R^a)-C(O)-C(O)-, -S-,
-S(O)-, -S(O)2-, -N(R^a)-S(O)2-, -S(O)2-N(R^a)-, -O-S(O)2-, -S(O)2-O-, -C(NH)-, and
-C(NOH)-; and

15 E³ is heterocyclyl optionally is substituted with one or more substituents
independently selected from the group consisting of halogen, hydroxy, cyano, carboxy,
thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, amino (optionally substituted with up to two
substituents independently selected from alkyl and carbocyclylalkyl), alkyl, alkoxy,
alkylthio, carbocyclyl, and carbocyclylalkyl, wherein:

20 any member of such group optionally is substituted with one or more
substituents independently selected from the group consisting of halogen, hydroxy,
cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, imino, aminocarbonyl, and
amino; and

each R^a is independently selected from the group consisting of hydrogen, hydroxy,
alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, bisalkoxyalkyl, alkylthioalkyl,
25 alkylthioalkenyl, alkylsulfoxidoalkyl, alkylsulfonyl, alkylsulfonylalkyl, carbocyclyl,
carbocyclylalkyl, carbocyclxyalkyl, carbocyclalkoxyalkyl, carbocyclthioalkyl,
carbocyclthioalkenyl, carbocyclsulfoxidoalkyl, carbocyclsulfonyl,
carbocyclsulfonylalkyl, heterocyclyl, heterocyclalkyl, heterocyclxyalkyl,
heterocyclalkoxyalkyl, heterocyclthioalkyl, heterocyclsulfoxidoalkyl,
30 heterocyclsulfonyl, heterocyclsulfonylalkyl, aminoalkyl, aminosulfonyl,

aminoalkylsulfonyl, and alkoxyalkylaminoalkyl, wherein any member of such group optionally is substituted:

on any carbon atom(s) capable of such substitution with one or more substituents independently selected from the group consisting of halogen, hydroxy, cyano, carboxy, thiol, sulfo, nitro, nitroso, oxo, thioxo, and imino, and

5 on any amino nitrogen atom with up to 2 substituents independently selected from the group consisting of alkyl, alkylcarbonyl, carbocyclyl, and carbocyclylalkyl.

10 16. A compound or salt thereof according to claim 15, wherein A¹ and A², together with the carbon to which they are bonded, form heterocyclyl or carbocyclyl, wherein:

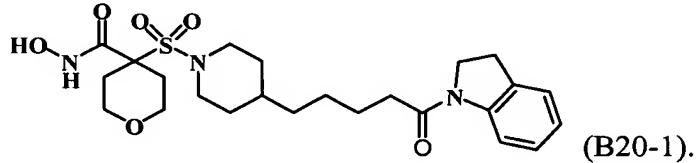
the heterocyclyl and carbocyclyl optionally are substituted with up to 3 independently selected R^X substituents.

15 17. A compound or salt thereof according to claim 16, wherein E¹ is alkenyl.

18. A compound or salt thereof according to claim 16, wherein E¹ is alkyl.

20 19. A compound or salt thereof according to claim 18, wherein E² is -C(O)-.

20. A compound or salt thereof according to claim 19, wherein the compound corresponds in structure to the following formula:



the method comprises administering a compound or a pharmaceutically acceptable salt thereof in a therapeutically-effective amount to the mammal; and
the compound is selected from the group of compounds recited in claim 1.

5 22. A method for treating a pathological condition in a mammal, wherein:
 the method comprises administering a compound or a pharmaceutically acceptable salt thereof in a therapeutically-effective amount to the mammal; and
 the compound is selected from the group of compounds recited in claim 1; and
 the pathological condition is selected from the group consisting of tissue
10 destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease, and a central nervous system disease.

15 23. A method for treating a pathological condition in a mammal, wherein:
 the method comprises administering a compound or a pharmaceutically acceptable salt thereof in a therapeutically-effective amount to the mammal; and
 the compound is selected from the group of compounds recited in claim 1; and
 the pathological condition is selected from the group consisting of osteoarthritis, rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor
20 angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction, coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, and
25 chronic obstructive pulmonary disease.

30 24. A method for treating a condition associated with pathological matrix metalloprotease, aggrecanase, or TNF- α convertase activity in a mammal, wherein:
 the method comprises administering a compound or a pharmaceutically acceptable salt thereof in a therapeutically-effective amount to the mammal; and

the compound is selected from the group of compounds recited in claim 15.

25. A method for treating a pathological condition in a mammal, wherein:
the method comprises administering a compound or a pharmaceutically acceptable

5 salt thereof in a therapeutically-effective amount to the mammal; and
the compound is selected from the group of compounds recited in claim 15; and

the pathological condition is selected from the group consisting of tissue
destruction, a fibrotic disease, matrix weakening, defective injury repair, a cardiovascular
disease, a pulmonary disease, a kidney disease, a liver disease, an ophthalmologic disease,
10 and a central nervous system disease.

26. A method for treating a pathological condition in a mammal, wherein:

the method comprises administering a compound or a pharmaceutically acceptable
salt thereof in a therapeutically-effective amount to the mammal; and

15 the compound is selected from the group of compounds recited in claim 15; and
the pathological condition is selected from the group consisting of osteoarthritis,

rheumatoid arthritis, septic arthritis, tumor invasion, tumor metastasis, tumor
angiogenesis, a decubitis ulcer, a gastric ulcer, a corneal ulcer, periodontal disease, liver
cirrhosis, fibrotic lung disease, otosclerosis, atherosclerosis, multiple sclerosis, dilated
20 cardiomyopathy, epidermal ulceration, epidermolysis bullosa, aortic aneurysm, defective
injury repair, an adhesion, scarring, congestive heart failure, post myocardial infarction,
coronary thrombosis, emphysema, proteinuria, Alzheimer's disease, bone disease, and
chronic obstructive pulmonary disease.

25 27. A pharmaceutical composition comprising a therapeutically-effective
amount of a compound or a pharmaceutically-acceptable salt thereof, wherein the
compound is selected from the group of compounds recited in claim 1.

28. A pharmaceutical composition comprising a therapeutically-effective amount of a compound or a pharmaceutically-acceptable salt thereof, wherein the compound is selected from the group of compounds recited in claim 15.